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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,206	01/02/2002	Jasper Rine	UOCB118456	1317

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EXAMINER	
BRUSCA, JOHN S	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 08/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/038,206	RINE ET AL.	
	Examiner	Art Unit	
	John S. Brusca	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2006*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38-85* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/9/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. In view of the withdrawal of the rejection for lack of written description noted below, priority is granted for the instant claims to the earliest priority date of parent Application No. 08/512,753.

Specification

2. The objections to the specification noted in the Office action mailed 07 March 2006 regarding improper incorporation by reference of essential subject matter, lack of antecedent basis of claimed subject matter, and an incorrect citation of Fodor et al. is withdrawn in view of the amendment to the specification filed 09 June 2006 and the applicant's pointing in page 16 of their response filed 09 June 2006 of support for probes with predetermined sequences of nucleotides at page 14, lines 24-32 of the specification.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claim 69 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 69 is drawn to data in computer readable memory which is not patentable subject matter (see MPEP 2106).

5. Applicant's arguments in the appeal brief filed 09 June 2006 have been fully considered but they are not persuasive. The applicants cite the MPEP statement that functional descriptive

material in a computer readable medium becomes statutory subject matter. However the amendment to claim 69 filed 09 June 2006 does not overcome the rejection under 35 U.S.C. 101 because the amendment to the limitations of the database data does not serve to convert the data into functional descriptive material. The claim remains drawn to data rather than a program that affects how a computer processes data. The applicants state that the claim as amended is drawn to a data structure and cite In re Lowry, however the claim is not drawn to a file structure format that is generic to the data content as in In re Lowry. The claim is drawn to a genus of data, and the rejection is maintained.

Claim Rejections - 35 USC § 112

6. The rejection claims 38-85 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement in the Office action mailed 07 March 2006 is withdrawn in view of the applicants pointing to support at page 14, lines 24-32 for probes with a predetermined sequence.

Claim Rejections - 35 USC § 102

7. The rejection of claims 38-53, 55-66, and 68-83, and 85 under 35 U.S.C. 102(a) and 35 U.S.C. 102 (e) as being anticipated by Fodor et al. '01 (U.S. Patent No. 6,309,822) in the Office action mailed 07 March 2006 is withdrawn in view of the perfection of the claim for priority to Application No. 08/512,753, filed 09 August 1995 noted above.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 38-53, 55-66, 68-83, and 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gress et al. in view of Granelli-Piperno et al. in view of either Fodor et al. '98 (U.S. Patent No. 5,800,992) or Fodor et al. '91 (reference 9 in the Information Disclosure Statement filed 20 November 2002).

The claims are drawn to a method of assay of the response of a living thing to a stimulus by use of an array of probes comprising a predetermined sequence of nucleotides to individual gene transcripts by comparing databases comprising results of hybridizations of labeled polynucleotides derived from cells either treated with different stimuli or unstimulated control cells, the database produced by the method, and methods of generating the database produced by the method. The responses are measured by converting an output signal to an electrical signal

and then converting the electrical signal to a value in a database. In some embodiments at least 50% of the gene transcripts of the cell are assayed, the cells are human cells, the probes consist of 24-240 nucleotides, and the database is computer implemented. In some embodiments the probes are in an X and Y coordinate grid. In some embodiments the method is repeated for different stimuli.

Gress et al. shows throughout, and especially on page 609 and figure 3 a general method of assaying patterns of transcription by use of labeled cDNA from mouse, and human cells by use of a cDNA X-Y coordinate grid array of probes. The array provides an optical signal of expression in an assayed human cell of individual genes in the cell. Gress et al. shows importing the resulting data via an electrical signal of a Phosphorimager to a computer implemented relational database on page 616. Gress et al. shows in the abstract that their high density array allows for the efficient assay of thousands of clones simultaneously. Gress et al. shows on page 612 that polyA control probes hybridize non-specifically to many array cDNA probes and that other cDNA probes in the array contained repetitive sequences that also caused non-specific hybridization. Gress et al. shows on page 616 that one strategy to avoid background non-specific hybridization is to use probes that lack polyA tails by use of modified primers. Gress et al. does not show subjection of assayed cells to different stimuli, or comparison of the transcriptional profile of cells that have received different stimuli, or assay of discrete portions of the complete number of genes of the cell, or use of probes with a predetermined sequence of nucleotides.

Granelli-Piperno et al. shows in figures 1-9 the effect of a variety of compounds on expression of genes of human cells. The tested compounds include cytokines, mitogens,

cyclosporin A, and cycloheximide. The response is determined by the intensity of a film image on an autoradiograph. Granelli-Piperno et al. show that assay of expression of genes after treatment of cells with drugs allows a determination of the effect of the drug on individual gene expression and further serves to gain insights on the mechanism of action of the drug.

Fodor et al.'98 shows throughout a method of making an array of polynucleotide probes of predetermined sequence by independent in situ stepwise synthesis of each oligonucleotide probe on the array. Fodor et al. '98 shows in columns 32, lines 12-24 that their arrays may be used to map the location of a molecule on a chromosomal map. Fodor et al. '98 shows in column 35 that their procedure may be used to assay the developmental stage cells from which the assayed sample is derived. In column 78-79, Fodor et al. '98 shows that their method may be used to assay developmental stages of cells by assay of their mRNA content.

Fodor et al. '91 shows in the abstract and pages 771-772 a method of synthesizing a dinucleotide of a predetermined sequence by a photolithographic process. Fodor et al. '91 concludes on page 772 that oligonucleotide arrays that could be made by their method would be useful to detect complementary sequences in RNA and DNA, and could be used for gene mapping, fingerprinting, and diagnostics.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Gress et al. by assaying cells that have received treatments with different drugs according to the method of Granelli-Piperno et al. because Granelli-Piperno et al. shows that such an analysis serves to gain insights on the mechanism of action of the drug. It would have been further obvious to assay additional numbers of genes as

desired to determine the effect of a drug on additional genes. Regarding the size of the probes, it would have been obvious to use portions of a cDNA probe of Gress et al. because Gress et al. shows that many array probes suffer from non-specific hybridization due to repetitive sequences of polyA tracts and that the problem may be solved by use of shorter probes. It would have been further obvious to make and use an array of probes with a predetermined sequence made by the methods disclosed by Fodor et al. '98 or Fodor et al. '91 because Fodor et al. '98 and Fodor et al. '91 show that such an array has the advantage of allowing the sequences detected in the sample to be mapped to a particular location of the genome of the organism sampled. Regarding the limitations of claims 71 and 72, it would be further obvious to one of skill in the art to perform simple mathematical comparisons of the levels in stimulated and control cells such as subtraction or division by the basal level to reveal the extent of change in the level of the assayed mRNA.

11. Claims 38, 49-51, 54, 56, 63-65, 67, 70, 80-82, and 84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gress et al. in view of Granelli-Piperno et al. in view of either Fodor et al. '98 or Fodor et al. '91 as applied to claims 38-53, 55-66, 68-83, and 85 above, and further in view of Watson et al.

The claims are drawn to assays utilizing fungal cells.

Gress et al. in view of Granelli-Piperno et al. in view of either Fodor et al. '98 or Fodor et al. '91 as applied to claims 38-53, 55-66, 68-83, and 85 above does not show assay of fungal cells.

Watson et al. shows on pages 573-575 that yeast cells contain genes that are regulated by stimuli such as metabolites.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of Gress et al. in view of Granelli-Piperno et al. in view of either Fodor et al. '98 or Fodor et al. '91 as applied to claims 38-53, 55-66, 68-83, and 85 above by using yeast gene probes and cells because Watson et al. shows that yeast cells have genes that are regulated by stimuli.

12. Applicant's arguments filed 09 June 2006 have been fully considered but they are not persuasive. The applicants state that Gress et al. teaches away from quantification of gene expression due to the necessity of controls, background from polyA tails and repeated sequences, and their intent to distinguish high level expression from medium levels of expression. However, Gress et al. shows that despite the necessity of controls it is possible to quantify levels of gene expression by their method, as shown in figure 2 and Table 1. The applicants state the Gress et al. teaches away from comparing stimulated cells and unstimulated cells, but do not point to a location in Gress et al. that supports their contention. The applicants state that Granelli-Piperno et al. does not cure all the deficiencies of Gress et al. noted above, however the applicants do not appear to argue that Granelli-Piperno et al. fail to show comparison of stimulated and unstimulated cells, for which the reference is relied upon in the rejection detailed above. The applicants argue that Fodor '91 is not combinable with Gress et al. because the use of predetermined sequences of probes shown in Fodor '91 would make Gress et al. inoperable. However the use of predetermined sequences of probes allows for use of the array of Gress et al. for additional purposes such as mapping locations of molecules, identify developmental stages of cells from which the samples are derived, and other information about the molecules that

hybridize to the array, as shown in Fodor '98 and Fodor '91. The modification of the array of Gress et al. by use of predetermined sequences of probes does not conflict with the purpose of Gress et al. of using the array for identification of highly expressed cDNA clones. Arrays with probes having predetermined sequences are more versatile and useful than the array of Gress et al. because they can be used for additional purposes without preventing their use in the method shown by Gress et al. The applicants state there is no motivation to combine the cited references, but the motivation to combine is discussed in the above rejection.

Conclusion

13. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John S. Brusca whose telephone number is 571 272-0714. The examiner can normally be reached on M-F 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

John S. Brusca 15 Sept 2006

John S. Brusca

Primary Examiner

Art Unit 1631

jsb